

AMENDMENT AND RESPONSE UNDER 37 CFR § 1.111  
Serial Number: 09/464158  
Filing Date: December 16, 1999  
Title: ASSAY FOR CARBOHYDRATE-FREE TRANSFERRIN

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### REMARKS

Claims 1 and 10 are amended, and claims 18-23 are added. As a result, claims 1-23 are now pending in this application. Claims 13-17 have been withdrawn from Examination. The amendments to claims 1 and 10 and new claims 18-23 are supported by the application as filed, and no new matter has been added.

The amendments to claims 1 and 10 are supported, for example, by the specification at page 8, third and fourth full paragraphs.

New claims 18-23 are supported, for example, by originally-filed claim 1, by the specification at pages 6-8., and by the specification at page 21, third paragraph.

#### I. The Interview Summary

Applicant would like to thank Examiner Hines for the courtesy extended during the telephonic interview on August 18, 2003. Applicant's attorneys Ann Viksnins and Peter Malen participated in the interview with Examiner Hines.

The Office Action mailed February 26, 2003, pending claims, and cited art were discussed during the interview. Applicant agreed to summarize the interview in this response.

Examiner Hines agreed that the Office Action mailed on February 26, 2003 would be treated as a non-final Office Action. This agreement confirmed the replacement "Office Action Summary" for the February 26, 2003 Office Action, faxed by Examiner Hines to Peter Malen on March 27, 2003 (a copy is enclosed herewith).

The above account is believed to be a complete and accurate summary of the interview as required by 37 C.F.R. § 1.133. If the Examiner believes that this summary is inaccurate or incomplete, Applicant respectfully requests that the Examiner point out any deficiencies in her next communication so that Applicant can amend or supplement the interview summary.

#### II. The 35 U.S.C. § 112, Second Paragraph, Rejections of the Claims

The Examiner rejected claims 1-12 under 35 USC § 112, second paragraph, alleging that those claims are incomplete for omitting essential steps (see item 7 of the Office Action on page 3). The Examiner also rejected claims 1-12 under 35 USC § 112, second paragraph, alleging that those claims are indefinite for failing to particularly point out and distinctly claim the subject matter which

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applicant regards as the invention (see item 9 of the Office Action on page 6). Claim 1 is amended to recite the phrase "wherein said content of carbohydrate free transferrin is used in the assessment of elevated alcohol consumption " and to recite "detecting the content of carbohydrate-free transferrin in said fraction", thereby rendering these rejections moot.

Thus, it is submitted that the pending claims are in conformance with the requirements of 35 U.S.C. § 112, second paragraph. Therefore, withdrawal of the rejections of the claims under 35 U.S.C. § 112, second paragraph, is appropriate and respectfully requested.

### III. The 35 U.S.C. § 112, First Paragraph, Rejections of the Claims

The Examiner rejected claims 3 and 5 under 35 U.S.C. § 112, first paragraph, alleging that the written description is not commensurate in scope with the claims. Specifically, the Examiner alleged that the phrase "and mixtures thereof" in claims 3 and 5 does not satisfy the written description requirement. Applicant respectfully traverses this rejection.

To satisfy the written description requirement, an Applicant's specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicant was legally in possession of the elements of the invention sought to be patented, i.e., whatever is claimed. M.P.E.P. §2163; *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997); *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991).

A patent application need not teach, and preferably omits, what is well known in the art. "Guides for Examination of Patent Applications under the 35 U.S.C. § 112, ¶ 1 'Written Description' Requirement," 66 *Fed Reg* 1099, 1105 (2001). (The absence of definitions or details for well-established terms should not be the basis for rejection for lack of adequate written description); *Spectra-Physics Inc. v. Coherent Inc.*, 827 F.2d 1524, 3 U.S.P.Q.2d 1737 (Fed. Cir. 1987). In other words, the sufficiency of the specification must be evaluated from the viewpoint of one skilled in the art, who is also in possession of all of the relevant prior art. Applicant respectfully asserts that the claimed invention has been described with sufficient particularity.

Claim 3 recites "[t]he method as claimed in claim 1, wherein the carbohydrate-binding ligand is selected from the group consisting of antibodies, antibody fragments, lectins, mammalian carbohydrate-binding proteins, microbial carbohydrate-binding proteins, and mixtures thereof.

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Claim 5 recites "[t]he method as claimed in claim 1, wherein the carbohydrate-binding ligand is selected from the group consisting of *Sambucus nigra* lectin, *Sambucus sielbodiana* lectin, wheatgerm agglutinin, *Muackia amurensis* lectin, *E. coli* K99 lectin, *Helicobacter pylori* lectin, *Ricinus communis* lectin, *Crotalaria junctae* lectin, anti-sialic acid antibodies, and mixtures thereof.

The Examiner's attention is first respectfully drawn to originally-filed claims 3 and 5. While these claims have been previously amended, originally-filed claims 3 and 5 recite that the carbohydrate-binding ligand is selected from a group of carbohydrate binding ligands, "and mixtures thereof". The Examiner's attention is also drawn the second full paragraph on page 9 of the specification for a detailed discussion of carbohydrate-binding ligands that may be used. This discussion of the carbohydrate-binding ligands extends through page 12 of the specification. As is stated at page 9, second full paragraph of the specification, carbohydrate-binding ligands "are known in the art and are widely described in the literature." Furthermore, as is stated in the specification, for example at the final paragraph of page 10, Applicant has also described that "more than one such binding ligand may be used".

Therefore, after considering both the disclosures in the specification, and also the information known to the art worker, Applicant respectfully asserts that the specification does convey with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicant was legally in possession of the elements of the invention sought to be patented. Thus, it is submitted that the 35 U.S.C. § 112, first paragraph, written description requirement has been met. Therefore, the Examiner is respectfully requested to withdraw the written description rejection of the claims.

#### IV. The 35 U.S.C. §§ 102(b) and 103(a) Rejections of the Claims

The Examiner rejected claims 1-3, 6-8 and 10-12 under 35 USC § 102(b), alleging that those claims are anticipated by Sundrehagen (WO 91/19983; hereinafter Sundrehagen). The Examiner also rejected claims 4-5 under 35 USC § 103(a), alleging that those claims are unpatentable over Sundrehagen in view of Pekelharing *et al.*, (*Analytical Biochemistry*, 165, 320 (1987); hereinafter Pekelharing). The Examiner also rejected claim 9 under 35 USC § 103(a) alleging that that claim is unpatentable over Sundrehagen in view of Dreher *et al.* (Canadian Patent No. 2,074,345; hereinafter Dreher). As these rejections may be maintained with respect to the pending claims, they are respectfully traversed.

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A. The 35 U.S.C. § 102(b) Rejection of the Claims

The Examiner rejected claims 1-3, 6-8 and 10-12 under 35 USC § 102(b), alleging that those claims are anticipated by Sundrehagen.

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Dillon*, 919 F.2d 688, 16 U.S.P.Q.2d 1897, 1908 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991). For anticipation, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the art. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 101 (Fed. Cir. 1991). To overcome the defense of anticipation, "it is only necessary for the patentee to show some tangible difference between the invention and the prior art." *Del Mar Engineering Lab v. Physio-Tronics, Inc.*, 642 F.2d 1167, 1172, (9<sup>th</sup> Cir. 1981).

Independent claim 1 recites "[a] method for the assessment of elevated alcohol consumption, said method comprising (a) contacting a sample of a body fluid with a carbohydrate-binding ligand, to bind any carbohydrate or carbohydrate-containing moieties in said sample to said ligand; (b) separating a carbohydrate-free transferrin containing fraction not binding to said ligand and contacting the separated fraction with an anti-transferrin antibody or an anti-transferrin antibody fragment; and (c) detecting the content of carbohydrate-free transferrin in said fraction and thereby determining the content of carbohydrate-free transferrin in said sample, wherein said content of carbohydrate free transferrin is used in the assessment of elevated alcohol consumption." Claims 2-12 depend either directly or indirectly from claim 1.

The Examiner's attention is initially respectfully directed to page 7, second full paragraph of the specification, where Applicant defines carbohydrate-free transferrin molecules as molecules of transferrin that are free of carbohydrate. This contrasts with transferrin preparations containing transferrin molecules, as discussed later in the same paragraph. These transferrin preparations may contain different percentages of carbohydrate-free transferrin molecules. Thus, the percentages (at least 60%; at least 70 or 80%; 90 or 95%) refer to the percentages of the transferrin molecules in the preparations that are carbohydrate-free transferrin molecules.

Sundrehagen

Sundrehagen discloses a method of binding fluorescein-labeled anti-transferrin antibodies to a population of transferrin molecules and separating transferrin molecules having two or fewer sialic

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acid residues (carbohydrate-deficient transferrin) from transferrin molecules with three or more sialic acid residues (*see* Example 7, page 22). Separation is performed via anion exchange resins at specific pH and buffering salt concentrations and compositions where the antigen-antibody complexes of transferrin variants with three or more sialic acid residues bind to the anion exchange solid phase, as opposed to the antigen-antibody complexes of transferrin variants having 2 or less sialic acid residues, which do not (page 12, final paragraph). Sundrehagen teaches that "it has been found important that the analyte variants [of transferrin] are reacted with a population of labeled binding partners which are reactive to all the different analyte variants to be analyzed" (page 4, lines 30-34; emphasis added; also see page 18, lines 25-28).

In contrast to claim 1, Sundrehagen does not disclose or suggest that specific measurement of transferrin molecules free of carbohydrate could be useful in the assessment of elevated alcohol consumption. Sundrehagen only discloses the measurement of carbohydrate deficient transferrin molecules. Furthermore, Sundrehagen relates to the use of antibodies to transferrin and does not teach or suggest the use of a carbohydrate-binding ligand to bind any carbohydrate or carbohydrate-containing moiety in a sample. Moreover, while Sundrehagen discloses that it is important that the transferrin variants are reacted with a population of labeled binding partners which are reactive to all the different variants of transferrin, the present invention is directed to a method where only those transferrin molecules having a carbohydrate binding moiety are bound to the carbohydrate-binding ligand. This allows the carbohydrate-free transferrin containing fraction to be separated from the transferrin molecules having carbohydrates. In the present invention, it is this carbohydrate-free transferrin containing fraction that is contacted with an anti-transferrin antibody or an anti-transferrin antibody fragment to detect the content of the carbohydrate free transferrin in the fraction. Thus, Sundrehagen does not anticipate claim 1 because it does not disclose every element of claim 1. Because claims 2-12 depend either directly or indirectly from claim 1, Sundrehagen does not anticipate those claims.

#### Conclusion

Applicant submits that Sundrehagen does not anticipate the claims because it does not disclose every element of a claim under consideration. Accordingly, the Examiner is respectfully requested to withdraw the rejections of the claims under 35 U.S.C. § 102(b).

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B. The 35 U.S.C. § 103(b) Rejection of the Claims

The Examiner rejected claims 4-5 under 35 USC § 103(a), alleging that those claims are unpatentable over Sundrehagen in view of Pekelharing. The Examiner also rejected claim 9 under 35 USC § 103(a) alleging that that claim is unpatentable over Sundrehagen in view of Dreher.

To establish a *prima facie* case of obviousness, the Examiner has the burden to establish three basic elements. First, the Examiner must establish that there is some suggestion or motivation, either in the cited documents themselves or in the knowledge generally available to an art worker, to modify the documents or to combine document teachings so as to arrive at the claimed invention. Second, the Examiner must establish that there is a reasonable expectation of success. Finally, the Examiner must establish that the prior art documents teach or suggests all the claim limitations. M.P.E.P. § 2143. Applicant respectfully asserts that the cited documents fail to teach or suggests all the claim limitations. Thus, Applicant respectfully submits that the claims are not *prima facie* obvious in view of the cited documents.

Pekelharing

The Examiner rejected claims 4-5 under 35 USC § 103(a), alleging that those claims are unpatentable over Sundrehagen in view of Pekelharing. Claim 4 recites "[t]he method as claimed in claim 1, wherein in step (a) a panel of more than one type of lectin is used as a carbohydrate binding ligand." Claim 5 recites "[t]he method as claimed in claim 1, wherein the carbohydrate-binding ligand is selected from the group consisting of *Sambucus nigra* lectin, *Sambucus sielbodiana* lectin, wheatgerm agglutinin, *Maackia amurensis* lectin, *E. coli* K99 lectin, *Helicobacter pylori* lectin, *Ricinus communis* lectin, *Crotalaria junctae* lectin, anti-sialic acid antibodies, and mixtures thereof."

Pekelharing discloses a sandwich immunoassay using immobilized antitransferrin antibodies or immobilized lectin. Pekelharing specifically relates to the use of an antitransferrin antibody immobilized on a solid phase to bind transferrin molecules from a sample (page 321, column 2, final paragraph). Once transferrin is bound to the immobilized antibody, biotinylated *R. communis* lectin is added, and the absorbance is read.

5/2/01  
In contrast to the methods of the present invention, the methods of Pekelharing do not involve separating a carbohydrate-free transferrin containing fraction not binding to a carbohydrate-binding ligand and contacting the separated fraction with an anti-transferrin antibody or an anti-transferrin antibody fragment. As the Examiner acknowledged in the Office Action mailed March

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23, 2001, Sundrehagen does not teach the use of lectins as carbohydrate-binding ligands. As discussed hereinabove, Sundrehagen also does not teach or suggest the use of a carbohydrate-binding ligand to bind any carbohydrate or carbohydrate-containing moiety in a sample. Nor does Sundrehagen involve separating a carbohydrate-free transferrin containing fraction not binding to a carbohydrate-binding ligand and contacting the separated fraction with an anti-transferrin antibody or an anti-transferrin antibody fragment. Thus, Applicant respectfully asserts that the combination of Sundrehagen and Pekelharing fails to teach or suggests all the claim limitations of any of the pending claims.

#### Dreher

The Examiner also rejected claim 9 under 35 USC § 103(a) alleging that claim is unpatentable over Sundrehagen in view of Dreher. Claim 9 recites "[t]he method as claimed in claim 1, wherein determining the transferrin content in step (c) is achieved by turbidometric or nephelometric means."

Dreher discloses methods for the turbidimetric or nephelometric determination of polypeptides in liquids. Dreher does not teach or suggest separating a carbohydrate-free transferrin containing fraction not binding to a carbohydrate-binding ligand and contacting the separated fraction with an anti-transferrin antibody or an anti-transferrin antibody fragment. The Examiner relies on Dreher only to allege that no more than routine skill would have been required to use immunoturbimetry and immunonephelometry in the method of assessment of transferrin as taught by Sundrehagen. Thus, it is respectfully submitted that any suggestion of immunoturbimetry and immunonephelometry in Dreher does not render the claims *prima facie* obvious over the combination of Sundrehagen and Dreher. Thus, Applicant respectfully asserts that the combination of Sundrehagen and Dreher fails to teach or suggests all the claim limitations of any of the pending claims.

#### Conclusion

Applicant submits that the cited documents, alone or in combination, fail to teach or suggests all the claim limitations of any of the pending claims. Specifically, none of the cited documents, alone or in combination, teach or suggest a method including the steps of contacting a sample of a body fluid with a carbohydrate-binding ligand to bind any carbohydrate or carbohydrate-containing moieties in the sample to the ligand, separating a carbohydrate-free transferrin containing fraction

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not binding to the ligand and contacting the separated fraction with an anti-transferrin antibody or an anti-transferrin antibody fragment; and detecting the content of carbohydrate-free transferrin in the fraction. Accordingly, Applicant respectfully submits that a *prima facie* case of obviousness has not been established, and the Examiner is respectfully requested to withdraw the rejections of the claims under 35 U.S.C. § 103(a).

### CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is requested. The Examiner is invited to telephone Applicant's attorney (612-371-2110) to facilitate prosecution of this application.

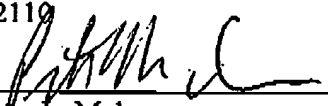
If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,  
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Date Aug 26, 2003

By

  
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